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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,077	03/12/2004	Ramachandra Reddy	VASG-P01-001	2078
28120	7590	07/08/2005	EXAMINER	
FISH & NEAVE IP GROUP ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			CHONG, KIMBERLY	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/800,077

Applicant(s)

REDDY ET AL.

Examiner

Kimberly Chong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-91 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-91 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                       |                                                                                        |
|-----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                      | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____                                                |

**0DETAILED ACTION**

***Election/Restrictions***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-29, 59 and 60, drawn to an isolated nucleic acid compound targeted to EphB4, classifiable in class 536, subclass 24.5.
- II. Claims 30-58, 59 and 60, drawn to an isolated nucleic acid compound targeted to EphrinB2, classifiable in class 536, subclass 6 and 24.5.
- III. Claims 61-62, 65-71, 73-77 drawn to a method of inhibiting EphB4 expression and treating a tumor or patient suffering from cancer comprising contacting the cell with a nucleic acid, classifiable in class 514, subclass 44.
- IV. Claims 63-70, 72-77 drawn to a method of inhibiting EphrinB2 expression in a cell and treating a tumor or patient suffering from cancer comprising contacting the cell with a nucleic acid, classifiable in class 514, subclass 44.
- V. Claims 78-83, drawn to a method for treating a patient suffering from an angiogenesis-associated disease comprising administering a nucleic acid targeted to EphB4, classifiable in class 514, subclass 44.
- VI. Claims 78-83, drawn to a method for treating a patient suffering from an angiogenesis-associated disease comprising administering a nucleic acid targeted to EphrinB2, classifiable in class 514, subclass 44.
- VII. Claims 84-85, drawn to the manufacture of a medicament for the treatment of cancer classifiable in class 435, subclass 6.

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- VIII. Claims 86-87, drawn to the manufacture of a medicament for treatment of an angiogenesis-associated disease, classifiable in class 435, subclass 6.
- IX. Claims 88 and 89, drawn to a method of identifying in a patient a plurality of cancer cells that express EphB4 and treating a patient suffering from such cancer, classifiable in class 514, subclass 44.
- X. Claims 88 and 89, drawn to a method of identifying in a patient a plurality of cancer cells that express EphrinB2 and treating a patient suffering from such cancer, classifiable in class 514, subclass 44.
- XI. Claims 90 and 91, drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 expression, classifiable in class 514, subclass 44.
- XII. Claims 90 and 91, drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphrinB2 expression, classifiable in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

Inventions of group I and group II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4 and group II is drawn to a nucleic acid inhibitor of EphrinB2,

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which are not disclosed as useful together and further are different molecules that target different genes. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product nucleic acid compound of group I can be used as a probe in *in situ* hybridization, which is materially different than the methods of inhibiting expression of a gene encoding EphB4 of group III. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group IV, which is drawn to a method of inhibiting expression of a gene encoding EphrinB2.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and

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a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product nucleic acid compound of group I can be used as a probe in *in situ* hybridization, which is materially different than the methods of treating a patient suffering from an angiogenesis-associated disease comprising administering a nucleic acid targeted to EphB4, as present in group V. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group VI, which is drawn to a method of treating a patient suffering from an angiogenesis-associated disease comprising administering a nucleic acid targeted to EphrinB2. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would

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not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group VII, which is drawn to the manufacture of a medicament for the treatment of cancer.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product nucleic acid compound of group I can be used as a probe in *in situ* hybridization, which is materially different than the methods of identifying a patient with a plurality of cancer cells that express EphB4 and treating a patient suffering from cancer comprising administering a nucleic acid targeted to EphB4, as present in group IX. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group X, which is drawn to a method of identifying a patient with a plurality of cancer cells that express EphrinB2 and treating a patient suffering from cancer comprising administering a nucleic acid targeted to EphrinB2. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.



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Inventions of group I and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group XI, which is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group I is drawn to a nucleic acid inhibitor of Eph4, which is not disclosed as capable of use in the invention of group XII, which is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphrinB2, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

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Inventions of group II and group III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group III, which is drawn to a method of inhibiting expression of a gene encoding EphB4. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product nucleic acid compound of group II can be used as a probe in *in situ* hybridization, which is materially different than the method of inhibiting expression of a gene encoding EphrinB2, as present in group IV. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

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operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group V, which is drawn to a method of treating a patient suffering from an angiogenesis-associated disease comprising administering a nucleic acid targeted to EphB4. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product nucleic acid compound of group II can be used as a probe in *in situ* hybridization, which is materially different than the method of treating a patient suffering from an angiogenesis-associated disease comprising administering a nucleic acid targeted to EphrinB2, as present in group VI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

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operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group VII, which is drawn to the manufacture of a medicament for the treatment of cancer. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have

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materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group IX, which is drawn to a method of identifying a patient with a plurality of cancer cells that express EphB4 and treating a patient suffering from cancer comprising administering a nucleic acid targeted to EphB4. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product nucleic acid compound of group II can be used as a probe in *in situ* hybridization, which is materially different than the methods of identifying a patient with a plurality of cancer cells that express EphrinB2 and treating a patient suffering from cancer comprising administering a nucleic acid targeted to EphrinB2, as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have

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materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group XI, which is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group II is drawn to a nucleic acid inhibitor of EphrinB2, which is not disclosed as capable of use in the invention of group XII, which is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphrinB2, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III-VI are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group III drawn to a method of

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inhibiting EphB4 in a patient suffering from cancer, group IV drawn to a method of inhibiting EphrinB2 in a patient suffering from cancer, group V drawn to a method of inhibiting Eph4 in a patient suffering from an angiogenesis-associated disease and group VI drawn to method of inhibiting EphrinB2 in a patient suffering from an angiogenesis-associated disease, are not disclosed as capable together and have different functions and effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group III is drawn to a method of inhibiting EphB4, which is not disclosed as capable of use in the invention of group VII, which is drawn to the manufacture of a medicament for the treatment of cancer. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have

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materially different modes of operation with different effects. For example, group III is drawn to a method of inhibiting EphB4, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of groups III and IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group III is drawn to a method of inhibiting expression of EphB4, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different functions and different effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.



Inventions of group IV-VI are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group IV drawn to a method of inhibiting EphrinB2 in a patient suffering from cancer, group V drawn to a method of inhibiting Eph4 in a patient suffering from an angiogenesis-associated disease and group VI drawn to method of inhibiting EphrinB2 in a patient suffering from an angiogenesis-associated disease, are not disclosed as capable together and have different functions and effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group IV is drawn to inhibiting EphrinB2 in a patient suffering from cancer, which is not disclosed as capable of use in the invention of group VII, which is drawn to the manufacture of a medicament for the treatment of cancer. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group IV is drawn to inhibiting EphrinB2 in a patient suffering from cancer, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of groups IV and IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group IV is drawn to inhibiting EphrinB2 in a patient suffering from cancer, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different

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functions and different effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group V drawn to a method of inhibiting Eph4 in a patient suffering from an angiogenesis-associated disease and group VI is drawn to method of inhibiting EphrinB2 in a patient suffering from an angiogenesis-associated disease, which are not disclosed as capable together and have different functions and effects.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group V is drawn to inhibiting EphB4 in a patient suffering from cancer, which is not disclosed as capable of use in the invention of group VII, which is drawn to the manufacture of a medicament for the treatment

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of cancer. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group V is drawn to inhibiting EphB4 in a patient suffering from cancer, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of groups V and IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group V is drawn to inhibiting EphB4 in a patient suffering from cancer, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a

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method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different functions and different effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group VI is drawn to method of inhibiting EphrinB2 in a patient suffering from an angiogenesis-associated disease, which is not disclosed as capable of use in the invention of group VII, which is drawn to the manufacture of a medicament for the treatment of cancer. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have

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materially different modes of operation with different effects. For example, group VI is drawn to method of inhibiting EphrinB2 in a patient suffering from an angiogenesis-associated disease, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of groups VI and IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group VI is drawn to method of inhibiting EphrinB2 in a patient suffering from an angiogenesis-associated disease, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different functions and different effects.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VII and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group VII is drawn to the manufacture of a medicament for the treatment of cancer, which is not disclosed as capable of use in the invention of group VIII, which is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease and additionally the methods have different functions and different effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of groups VIII and IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group VIII is drawn to the manufacture of a medicament for the treatment of an angiogenesis-associated disease, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is

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suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different functions and different effects.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of groups VIII and IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group VIII is drawn to the manufacture of a medicament for the treatment of an angiogenesis associated disease, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different functions and different effects.

Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.



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Inventions of groups IX-XII are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, group IX is drawn to a method of identifying a patient and treating a patient that expresses EphB4, group X is drawn to a method of identifying a patient and treating a patient that expresses EphrinB2, group XI is drawn to a method of identifying a tumor that is suitable for treatment with an inhibitor of EphB4 and group XII is drawn to identifying a tumor that is suitable for treatment with an inhibitor of EphB4, which are not disclosed as capable of use together and additionally, the methods have different functions and different effects. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

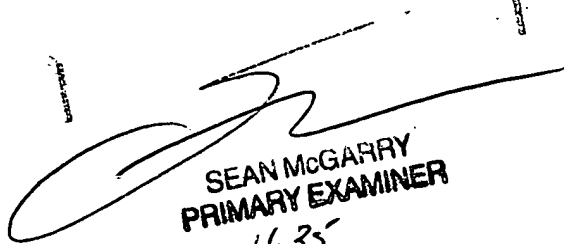
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong  
Examiner  
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